to your question I would say yes. If you want to go into the details of why we think so, it will take some development, but I would say yes.

Mr. GORDON. There is evidence that they did make it clear to the detail men?

Dr. MCCLEERY. There is indirect evidence that they did make it clear, yes.

Dr. MINCHEW. We were assured that this would be done. At the end of the meeting the senior Pfizer executive present, stated that in general the firm accepted FDA's proposals, and that the firm would prepare corrected copy for the visual aid and submit it to the Bureau of Medicine for approval as soon as possible.

Senator NELSON. This visual aid was to be used in detailing to physicians?

Dr. MINCHEW. Yes. Now, at this point in time the visual aid was going to be presented to the detail men themselves for instructional purposes for them, and then subsequently the visual aid would be used for the detail man's presentation to the physician.

Senator NELSON. All right.

Dr. MINCHEW. On September 11, 1967, Pfizer submitted a copy of the four-color printed visual aid with only some of the requested corrections pasted over the original copy. Several additional changes were considered necessary. Notable among these were: (1) The need to reduce from 754 to 454 the number of cases cited in a chart showing clinical success rate, since a number of the cases included by the company were not regarded as sufficiently documented; and, (2) The need to state clearly that claims for lower binding of calcium with Vibramycin were based only on in vitro studies.

These additional changes were discussed with Pfizer representatives, and they agreed to all of them. They were told that other promotional material, such as the file card, a booklet, and dosage calculator that Pfizer had presented, would have to be similarly revised before they were distributed.

In a letter dated September 14, 1967, Pfizer reflected its agreement with the changes we felt were necessary.

This submission is presented to you, and the paste over will show the necessary changes.[1]

A revised, final printed copy of the visual aid was submitted on October 6, 1967, and a copy of this has been submitted.[2] It was reviewed and found to contain all changes requested in the prior negotiations.

Let me again note two of the major corrections Pfizer was required to make in the Vibramycin visual aid: First, the company was required to indicate that the antibacterial spectrum of Vibramycin was not significantly different from other tetracyclines; second, the company was required to omit, because of a lack of supporting clinical evidence, any inference that the depicted in vitro test indicated there was less chance that Vibramycin will be deposited in the teeth and bones of children.

Very soon after the introduction of the new antibiotic, a pediatrician reported to the FDA by letter that at the American Academy of Pediatrics annual meeting at the Washington Hilton Hotel, on October 25, 1967, a Pfizer representative had stated that Vibramycin in vitro had the least calcium binding capacity, and that, based on this

[1] See information beginning at p. 3596, infra.
[2] See information beginning at p. 3619, infra.